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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,797	12/17/2003	Katherine Meyer Siegler	111828-00109	7390

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,797	SIEGLER, KATHERINE MEYER	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *6-10,16-22 and 24-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-15 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040503*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The election with traverse filed August 9, 2006, is acknowledged and has been entered.

Applicant has elected the invention of Group I, claims 2-5 and 11-15, drawn to a method for detecting or diagnosing prostate cancer in an individual, said method comprising determining the levels of MIF in the serum of the individual by immunoassay.

Claims 1 and 23 are linking claims, linking the inventions of Groups I and II, as identified by the Office action mailed July 21, 2006.

2. Claims 1-93 are pending in the application. Claims 6-10, 16-22, and 24-93 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 9, 2006.

3. Claims 1-5, 11-15, and 23 are currently under prosecution.

Information Disclosure Statement

4. The information disclosure filed May 3, 2004, has been considered. An initialed copy is enclosed.

Election/Restrictions

5. Applicant's traversal of the restriction and election requirement set forth in the preceding Office action mailed July 21, 2006, is acknowledged.

Applicant's arguments have been carefully considered but not found persuasive for the following reason:

Although, as Applicant has remarked, the inventions relate in some manner to the presence of MIF in the serum of individuals afflicted by prostate cancer, as explained in

the preceding Office action, the search required to consider claims directed to any one of the inventions is not the same, nor is it coextensive with the search required to consider claims directed to any other invention. Accordingly, contrary to Applicant's assertion, searching and considering claims directed to more than one of the inventions would constitute a serious burden.

Therefore, the restriction and election requirement is deemed proper and is made FINAL.

Specification

6. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of such an improperly demarcated trademark appearing in the specification is GenBank™ (see, e.g., paragraph [0065] of the published application[1]).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

(a) Claim 5 is directed to the method of claim 2, wherein the immunoassay is a protein array. At paragraph [0037] of the published application, the specification discloses the nucleic acid hybridization assay may involve the use of probes immobilized

[1] U.S. Patent Application Publication No. 2004/0171021 A1.

on solid supports, such as microarrays; but the specification does not describe an immunoassay that is, or comprises the use of a protein array.

(b) Claim 23 is directed to the method of claim 1, further comprising the step of comparing the levels of MIF in the serum of the individual to the MIF levels of prostate cancer patients. The specification, however, fails to provide proper antecedent basis for the claimed subject matter.

Claim Objections

8. Claims 1-5, 11-15, and 23 are objected to as being drawn to the subject matter of non-elected inventions (i.e., the inventions of Groups III and IV), which are not linked by the linking claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5, 11-15, and 23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, 11-15, and 23 are indefinite for the following reasons:

Claim 1 fails to recite a positive correlation step that clearly relates back to the objective of the invention, as recited in the preamble of the claim. The claim is directed to a method for detecting or diagnosing prostate cancer in an individual; yet, the claim merely recites the process comprises the step of determining levels of MIF in the serum of the individual. There is no process step that clearly relates back to the purpose or objective of the claimed invention; consequently, the skilled artisan could not determine whether each and every process step considered essential to the practice of the claimed invention has been included in the body of the claim. Thus, in the absence of a correlative step positively relating the whole of the process to its intended use, as recited in the preamble, the claim fails to delineate the subject matter that Applicant regards as the invention with the requisite degree of clarity and particularity to permit the skilled

artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhang et al. (*Hepatobiliary Pancreat. Dis. Int.* 2002 Nov; **1** (4): 577-580).

Zhang et al. teaches measuring the levels of MIF in the serum of individuals; see entire document (e.g., the abstract). Zhang et al. teaches the measurement was made using an ELISA; see, e.g., the abstract; and page 578, column 1.

13. Claims 1-3 and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Mitamura et al. (*Br. J. Ophthalmol.* 2000; **84**: 636-639).

Mitamura et al. teaches measuring the levels of MIF in the serum of individuals; see entire document (e.g., the abstract). Mitamura et al. teaches the measurement was made using an ELISA; see, e.g., the abstract; and page 637, paragraph bridging columns. Mitamura et al. teaches the ELISA utilized a biotin-labeled antibody that specifically binds MIF; see, e.g., page 637, column 2.

14. Claims 1, 2, 4, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Leech et al. (*Arthritis Rheumatol.* 2000 Apr; **43** (4): 827-833).

Leech et al. teaches measuring the levels of MIF in the serum of individuals; see entire document (e.g., the abstract). Leech et al. teaches the measurement was made using an immunblot (i.e., Western blot) assay; see, e.g., the abstract.

15. Claims 1-3, 11-15, and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Meyer-Siegler et al. (*Cancer.* 2002 Mar 1; **94** (5): 1449-1456) (of record; cited by Applicant).

Meyer-Siegler et al. teaches measuring the levels of MIF in the serum of individuals; see entire document (e.g., the abstract). Meyer-Siegler et al. teaches the measurement was made using an ELISA; see, e.g., the abstract; and page 1451, column 1. Meyer-Siegler et al. teaches the ELISA utilized a biotin-labeled antibody that specifically binds MIF; see, e.g., page 1451, column 1. Meyer-Siegler et al. teaches comparing the levels of MIF in the serum of an individual to the levels of MIF in prostate cancer patients; see, e.g., the abstract; page 1452, Figure 1; and page 1453, Table 1.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1, 2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitamura et al. (*Br. J. Ophthalmol.* 2000; **84**: 636-639) in view of Leech et al. (*Arthritis Rheumatol.* 2000 Apr; **43** (4): 827-833).

Here, claims 1, 2, and 4 are directed to the method of claim 4.

Mitamura et al. teaches that which is set forth in the above rejection of claims 1-3 and 11-15 35 U.S.C. 102(b).

Mitamura et al., however, does not teach measuring the levels of MIF in the serum of individuals using an immunblot assay.

Leech et al. teaches measuring the levels of MIF in the serum of individuals using an immunblot assay.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have measured the level of MIF in the serum of the individual

using an immunoblot assay because Leech et al. teaches such an assay is used to do so. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to determine the level of MIF in the serum of the individual.

18. Claims 1, 2, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitamura et al. (*Br. J. Ophthalmol.* 2000; **84**: 636-639) in view of Wright et al. (*Prostate Cancer Prostatic Dis.* 1999 Dec; **2** (5/6): 264-76).

Here, claims 1, 2, and 5 are directed to the method of claim 5.

Mitamura et al. teaches that which is set forth in the above rejection of claims 1-3 and 11-15 35 U.S.C. 102(b).

Mitamura et al., however, does not teach measuring the levels of MIF in the serum of individuals using a protein array.

Wright et al. teaches measuring the levels of serum biomarkers using a protein array; see entire document (e.g., the abstract). Wright et al. teaches improved early detection and diagnosis will require the use of such rapid and high throughput technology, which enables the detection of multiple markers; see, e.g., the abstract.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to have measured the level of MIF in the serum of the individual using a protein array because Wright et al. teaches the use of such arrays provides rapid and high throughput detection of multiple markers, which will improve early detection and diagnosis of disease associated with the presence of the markers in the serum. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to improve early detection and diagnosis of disease associated with the presence of the markers in the serum.

19. Claims 1-4, 11-13, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,043,044 A (of record; cited by Applicant) in view of Koong et al. (*Cancer Res.* 2000 Feb 15; **60**: 883-887) and Meyer-Siegler (*J. Interferon Cytokine Res.* 2000; **20**: 769-778).

U.S. Patent No. 6,043,044 A (Hudson et al.) teaches detecting and diagnosing prostate cancer in a subject by a process comprising measuring the levels of MIF within the subject's tissues or cells and comparing those levels to the levels of MIF in appropriate positive and/or negative control cells; see entire document (e.g., column 1, line 60, through column 2, line 24; column 2, lines 62-65; column 3, lines 1-25 and Table 1; and claims 1-3). Hudson et al. teaches the measurement is made using an ELISA or an immunoblot; see, e.g., column 4, lines 39-67; and column 5, lines 4-32. Hudson et al. teaches comparing the levels of MIF in the tissue or cell samples of an individual to the levels of MIF in prostate cancer patients; see, e.g., column 3, Table 1.

Hudson et al., however, does not teach detecting and/or diagnosing prostate cancer in a subject by measuring the levels of MIF within the subject's serum.

Koong et al. teaches MIF is overexpressed in cancer cells; see entire document (e.g., the abstract; page 885, Table 1; and page 886, column 1 and 2). Koong et al. teaches another protein, namely PAI-1, which is also overexpressed in cancer cells; see, e.g., page 885, Table 1. Koong et al. teaches because PAI-1 is a secreted protein, serum levels are readily detectable and may be used as a molecular marker; see, e.g., page 883, column 2. Moreover, Koong et al. teaches because PAI-1 is a secreted protein, serum levels can be monitored in a relatively noninvasive manner to determine or detect early subclinical recurrence of the disease associated with its overexpression; see, e.g., page 885, column 2. Koong et al. teaches measurements of the tumor antigens are made using an ELISA; see, e.g., page 884, the paragraph bridging columns.

Meyer-Siegler teaches prostate epithelial cells secrete MIF; see entire document (e.g., the abstract). Moreover, Meyer-Siegler teaches prostate cancer cells secrete more MIF than normal prostate cells; see, e.g., the abstract.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to have detected and/or diagnosed prostate cancer in a subject by measuring the levels of MIF within the subject's serum and comparing the determined levels to appropriate negative and/or positive controls, such as the levels of MIF in the sera of subject known not to have prostate cancer or the sera of subjects already diagnosed with prostate cancer, because Hudson et al. teaches MIF is

overexpressed in prostate cancer, as compared to normal prostate, Meyer-Siegler teaches MIF is secreted by prostate epithelial cells, including prostate cancer cells, which secrete relatively more MIF than normal prostate cells, and Koong et al. teaches since a tumor antigen, such as MIF, is overexpressed and secreted by cancer cells, its presence in the serum of subject's afflicted by the disease is readily determined. One ordinarily skilled in the art at the time the invention was made would have been motivated to do so to detect and/or diagnose prostate cancer in an individual, and more particularly because Koong et al. teaches the serum levels of such tumor antigens are monitored in a relatively noninvasive manner to permit determination or detection of early subclinical recurrence of the disease.

Conclusion

20. No claim is allowed.

21. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Arcuri et al. (*Prostate*. 1999; **39**: 159-165) teaches MIF is localized to the microvilli of the secretory luminal prostatic epithelium and secreted into all prostatic fluids examined; see entire document (e.g., page 163, column 1). Meyer-Siegler et al. (*Urology*. 1996; **48**: 448-452) teaches MIF is differentially expressed by prostate cancer cells, as compared to normal prostate cells; see entire document (e.g., the abstract; and page 451, column 1).

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
September 13, 2006